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# Response to Doherty et al: Early initiation of antiretroviral therapy amongst young children: a long way to go

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We thank Doherty and colleagues for their thoughtful and pertinent response to our manuscript describing trends in immunodeficiency at antiretroviral therapy (ART) initiation in children in low, middle and high income countries.[1] We agree that it is important to know more about the IeDEA sites included in the analysis in order to assess the extent to which they are representative of general public health facilities, and hence whether the finding of improvement in proportion of children with immunosuppression at ART initiation (albeit modest) is generalizable across these countries.

The IeDEA collaboration and the participating sites have therefore been described in dedicated profiles[2,3] and a survey of the IeDEA sites providing HIV care for children has been published.[4] The survey included 63 sites in Asia (10), Central Africa (4), East Africa (29), Southern Africa (10) and West Africa (10). Nearly 75% of sites were public government-run clinics, 65% were in urban settings and 57% provided pediatric care in combined adult-pediatric clinics.[4] As pointed out by Doherty and colleagues, many sites received additional financial support from research grants (57%), the US PEPFAR programme (54%) or the Global Fund (24%).[4] We cannot exclude that access to timely paediatric ART at non-IeDEA facilities may be even worse. However, all IeDEA sites

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followed the relevant national ART guidelines and a strength of IeDEA data is that it is collected as part of routine care and not from dedicated research cohorts. We believe that the availability of individualized data through the IeDEA collaboration allowed a more nuanced picture of pediatric ART than analyses of program-level aggregate data, while preventing the ecological bias that may affect aggregate data analyses.[5]

We concur with Doherty and colleagues regarding the importance of advocacy for pediatric HIV as a neglected disease with an urgent need for better access to diagnostic tests and effective and safe pediatric-friendly drug formulations.[6] The first barrier to early ART initiation is poor access to early infant diagnosis (EID) for which coverage remains low in many settings due to lack of virological diagnostic capacity, delivery services, and low social acceptability.[78] Even in IeDEA sites, EID for infants was not universally available throughout the period of data collection, with the diagnosis of HIV being dependent on the presence of clinical symptoms. In the IeDEA site survey, access to certain drugs especially as part of fixed-dose combinations was limited in certain regions.[4] Interestingly, Asian sites had poorer access to tenofovir and abacavir which may reflect more frequent eligibility for PEPFAR pricing in sub-Saharan Africa.[4] We have also previously found limited access to second-line options for children, which may result in delays or lack of switching to second-line therapy.[910] While the dramatically increased coverage and effectiveness of prevention of mother to child transmission programmes is to be welcomed, there is a risk of even further neglect of treatment options for children as the market diminishes in size. In addition, the low priority and complexity of conducting research in children means that there is limited high quality data from randomized clinical trials to inform optimal pediatric treatment guidelines and drug choices. We strongly endorse the call for better drug options for children, especially for very young infants where treatment options are extremely limited and we know that there is substantial mortality and morbidity benefit in starting ART before 3 months of age.[11]

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